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10/564,441	03/01/2006	Soren Persson	SSI7USA	7400

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HOWSON & HOWSON LLP
501 OFFICE CENTER DRIVE
SUITE 210
FORT WASHINGTON, PA 19034

EXAMINER	
HINES, JANA A	

ART UNIT	PAPER NUMBER
1645	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/564,441	PERSSON	
	Examiner	Art Unit	
	JaNa Hines	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 April 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,39,41-46,48-56 and 58-63* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *1,39,41-46,48-56 and 58-63* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *4/3/09*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Amendment Entry

1. The amendment filed April 3, 2009 has been entered. Claims 1, 39, 45, 48-54 and 58 have been amended. Claims 2-38, 40, 47 and 57 are cancelled. Claims 61-63 are newly added. Claims 1, 39, 41-46, 48-56, and 58-63 are under consideration in this office action.

Information Disclosure Statement

2. The information disclosure statement (IDS) submitted on April 3, 2009 was filed. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner.

Withdrawal of Objections and Rejections

3. The following objections and rejections have been withdrawn in view of applicants' amendments and arguments:

a) The objection of claim 1; and

b) The rejection of claims 40, 47, 49, 50, 53 under 35 U.S.C. 112, second paragraph.

Response to Arguments

4. Applicant's arguments filed April 3, 2009 have been fully considered but they are not persuasive.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 1, 39, 41-46, 48-56, and 58-63 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a) The rejection over preamble of the claim 1 is drawn to a screening method for simultaneous detection of diarrheagenic *Shigella* species and *E. coli* is maintained. While the examiners acknowledges the amendments to the claims, there is no correlation step which correlates the screening method for simultaneous detection of diarrheagenic *Shigella* species and *E. coli* to detecting the presence of one or more of the amplified genes and identifying subjects having the amplified genes. Therefore, the goal of the preamble is not commensurate with the steps of the method to thereby allow detection of diarrheagenic *Shigella* species and *E. coli*, when the method only recites identifying amplified genes.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. Claims 1, 39, 41-46, 48-56, and 58-63 are rejected under 35 U.S.C. 103(a) as being unpatentable over Toma et al., (J. of Clin. Microbiol. 2003. Vol. 41(6): 2669-2671) in view of Grabowski et al., (WO 02/053771 published July 7, 2002; however the US Patent Application Publication US 2004/0110251 will be used as the English translation).

The claims are drawn to a screening method for simultaneous detection of diarrheagenic *Shigella* species and *E. coli* (DEC) selected from the group consisting of one or more of Attaching and Effacing *E. coli* (A/EEC), Enteropathogenic *E. coli* (EPEC), Enterotoxigenic *E. coli* (ETEC), Verocytotoxin-producing *E. coli* (VTEC), Enteroinvasive *E. coli* (EIEC) and strains containing the *ehxA* gene, wherein said method comprises performing multiplex PCR by contacting a sample with multiple primers in a single reaction, wherein the multiple primers comprise at least one primer which specifically amplifies *vtxl* or a part thereof, at least one primer that specifically amplifies *vtx2* or a part thereof, at least one primer that specifically amplifies *ipaH* or a part thereof, at least one primer that specifically amplifies *eae* or a part thereof, at least one primer that specifically amplifies *estA* or *sta* or a part thereof, and at least one primer that specifically amplifies *elt* or a part thereof, wherein the primers are each independently selected from the group consisting of: a) the primers listed in Table 3; b) sequences having a sequence identity of at least 80% with a primer listed in Table 3; and c) a fragment of a primer listed in Table 3 comprising at least 10 nucleotides; and detecting the presence of the one or more amplified genes, and identifying subjects having the amplified genes. The dependant claims are gene to the

detection of specific genes; detection by electrophoresis; the sample source; and specific characteristics of the primer.

The claims are also drawn to a kit which comprises in a single or separate containers, nucleotide sequences which are able to prime amplify, in a nucleotide sequence amplification reaction the genes: *ipaH, eae, estA, vtx1, vtx2,* and elt or parts of these genes or the complementary strands to the genes or parts thereof wherein the nucleotide sequences for priming are selected from the group consisting of the priming sequences in Table 3 or sequences having at least 80% identity with the priming sequences in Table 3 and which comprises a control.

The rejection is on the grounds that it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention to combine the methods as taught by Toma et al., in view of Grabowski et al., and incorporate additional primers to amplify specific genes in order to provide a specific, practical and rapid diagnosis for identification of diarrheagenic *Shigella* and *E. coli*.

Response to Arguments

7. Applicant's arguments filed April 3, 2009 have been fully considered but they are not persuasive. The rejection of claims 1, 39, 41-46, 48-56, and 58-63 under 35 U.S.C. 103(a) as being unpatentable over Toma et al., in view of Grabowski et al., is maintained for reasons already of record.

Applicants argue that it would not have been obvious to one of skill in the art to combine the methods of Toma and Grabowski, because it is the simultaneous amplification and detection of the specific combination of genes that renders the screening method effective. In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, Both Toma et al., and Grabowski et al., teach performing multiplex PCR by contacting a sample with multiple primers in a single reaction wherein the multiple primers comprise primers which amplify the recited genes. Therefore Toma et al., and Grabowski et al., teach simultaneous amplification and detection of the specific combination of genes that renders the screening method effective, just as required by the claims.

Applicants argue that it is not proper for the Examiner to pick and choose some genes from each of the various references to arrive at Applicants method which uses impermissible hindsight knowledge. In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed

invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971). As is the case here, the rejection takes into account only knowledge which was clearly and expressly within the level of ordinary skill at the time the claimed invention was made. The references teach the various genes and primers were already known in the art, and the rejection does not include knowledge gleaned from the applicant's disclosure; therefore such a reconstruction is proper and applicants' argument is not persuasive.

Applicants assert that the combination of primers is not a random selection, but primers cable of functioning under PCR conditions. It is the offices position that Toma et al., teach multiplex PCR assays for identification of human diarrheagenic *E. coli* (DEC), enteropathogenic *E. coli* (EPEC), Enteroinvasive *E. coli* (EIEC), enterotoxigenic *E. coli* (ETEC), enteroaggregative *E. coli* (EAEC) and *Shiga* toxin producing *E. coli* (STEC). Toma et al., selected as targets, *eae* for EPEC and *bfpA* (which is known to be present in EPEC), *elt* and *est* for ETEC, and *ipaH* for EIEC wherein for each target, different but appropriate primers were selected. Similarly, Grabowski et al., teach VTEC is characterized as either possessing vtx1 and vtx2 genes. Therefore contrary to application's assertion random combinations of primers were not selected, rather the primers were each independently selected as specific targets of the identification/detection of specific *E. coli* and *Shigella* species. Furthermore, both Toma et al., and Grabowski et al., teach functioning multiplex PCR assays. Therefore applicants' argument is not persuasive in view of the prior art references teaching the

exact same performance of multiplex PCR steps, using the same primers listed in Table 3 and detecting the presence of those genes.

Applicants urge that sensitivity and specificity of the method are important aspects in detection of pathogenic microorganisms, since the template concentration is often very low in samples (e.g., in feces samples), and the number of non-target microorganisms is very high and that Applicants' primers disclosed in Table 3 have proven superior without losing specificity. However it is the position of the Office that Toma et al., teach using quite sensitive oligonucleotides within multiplex PCR techniques that avoids false negative and positive results while increasing sensitivity without comprising the specificity. Therefor the references address the sensitivity and specificity within the multiplex PCR assay. Furthermore, all of the claimed elements were known and disclosed by Toma et al., and Grabowski et al, and one skilled in the art could have combined the elements as claimed by known methods with no change in their respective functions, and the combination would have yielded predictable results to one of ordinary skill in the art at the time of the invention.

Applicants assert that neither Toma et al., nor Grabowski et al, describe the primers disclosed in Table 3. However the claims primers listed in Table 3; Toma et al., teach primers *eae, est, elt* and *ipaH* while Grabowski et al., teach *vtx1* and *vtx2* all of which are listed in Table 3, contrary to applicants statements.

Therefore, one of ordinary skill in the art at the time the invention was made would have been motivated to combine the methods taught by Toma et al., and Grabowski et al., in the screening method for simultaneous detection and identification

of subjects having amplified *vtx1, vtx2, ipaH, eae, estA* or *sta* and *elt* genes when both teach performing multiplex PCR with two or more primers in a single reaction for the identification of specific genes in order to provide a specific, sensitive, practical and rapid diagnosis for identification of diarrheagenic *Shigella and E. coli*. Thus applicants' arguments are not persuasive and the rejection is maintained.

Claim Rejections - 35 USC § 103

8. Claims 44, 50-53 and 58 are rejected under 35 U.S.C. 103(a) as being unpatentable over Toma et al., as applied to claims 1, 43 and 54 above, and further in view of Karube et al.

The rejection is on the grounds that it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention to combine the methods as taught by Toma et al., and Grabowski et al., and incorporate additional probes as taught by Karube et al., to in order to provide a screening method for simultaneous detection and identification of subjects having amplified *E.coli* genes when all the references teach performing PCR with a variety of probes and primers in a reaction for the identification of specific genes.

Response to Arguments

9. Applicant's arguments filed April 3, 2009 have been fully considered but they are not persuasive.

Applicants argue that Karube et al., adds nothing to Toma et al., and Grabowski et al., In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention to combine the methods as taught by Toma et al., and Grabowski et al., and incorporate additional probes as taught by Karube et al., to in order to provide a specific, practical and rapid diagnosis for identification of *E. coli*.

Applicants argue that the sequence of Karube et al., is part of a larger DNA sequences from Type II pathogenic verotoxin producing *E. coli*. However the claims are drawn to detecting Verotoxin producing *E. coli* (VTEC). Furthermore, the claims either require the probe having a sequence from Table 7; sequences having a sequence identity of at least 80%; or parts of the sequences having a length of more than 10 nucleotides; all of which Karube et al., teach. Thus, Karube et al., meet the limitations of the claims; especially since Applicant clearly state that the sequence of VTEC is not novel. Therefore, all of the claimed elements were known and disclosed by Toma et al., Grabowski et al, and Karube et al., therefore one skilled in the art could have combined the elements as claimed by known methods with no change in their respective

functions, and the combination would have yielded predictable results to one of ordinary skill in the art at the time of the invention. Thus applicants' arguments are not persuasive and the rejection is maintained.

New Grounds of Rejection

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 1, 39, 41-46, 48-56, and 58-63 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Neither the specification nor originally presented claims provides support for a screening method for simultaneous detection of diarrheagenic *Shigella* species and *E. coli* wherein the primers are each independently selected from a fragment of a primer listed in Table 3 comprising at least 10 nucleotides.

Applicant did not point to support in the specification for a screening method for simultaneous detection of diarrheagenic *Shigella* species and *E. coli* wherein the primers are each independently selected from a fragment of a primer listed in Table 3

comprising at least 10 nucleotides. Moreover, applicant failed to specifically point to the identity or provide structural characteristics of fragments of primers listed in Table 3 comprising at least 10 nucleotides. Thus, there appears to be no teaching of fragments of primers listed in Table 3 comprising at least 10 nucleotides.

Applicant has pointed to pages 1, lines 18-23, page 8, lines 8-11 of the instant specification and claim 47 for support of the amendment, however it appears that the entire specification appears to fail to recite support for the fragments of primers listed in Table 3 comprising at least 10 nucleotides. Therefore, it appears that there is no support in the specification. Thus, applicants must specifically point to page and line number support for the identity of a screening method for simultaneous detection of diarrheagenic *Shigella* species and *E. coli* wherein the primers are each independently selected from a fragment of a primer listed in Table 3 comprising at least 10 nucleotides. Therefore, the claims incorporate new matter and are accordingly rejected.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

11. Claims 1, 39, 41-46 and 48-53 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a) Claim 1 recites the limitation "the ehxA gene" in the claim. There is insufficient antecedent basis for this limitation in the claim.

Conclusion

12. No claims allowed.

13. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ja-Na Hines whose telephone number is 571-272-0859. The examiner can normally be reached Monday thru Thursday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Robert Mondesi, can be reached on 571-272-0956. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/JaNa Hines/
Examiner, Art Unit 1645

/Mark Navarro/

Primary Examiner, Art Unit 1645